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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/729,754	12/04/2000	Eugeni A. Vaisberg	CYTOP005	7528

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EXAMINER	
TABATABAI, ABOLFAZL	

ART UNIT	PAPER NUMBER
2625	14

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/729,754	VAISBERG ET AL.	
	Examiner	Art Unit	
	Abolfazl Tabatabai	2625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2000*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 December 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3,7,9,10,11,12,13*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Bacus et al (U S 5,281,517).

Regarding claim 1, Bacus discloses methods for immunoploidy analysis comprising:

receiving an image of the cell (column 4, lines 58-62), in which local values of a DNA image parameter correspond to amounts of DNA at the locations within the cell shown oil the image (column 7, lines 40-46); and,

estimating a total value of the DNA image parameter taken over at least a region of the cell where DNA is deemed to be present (see abstract and column 4, lines 41-47).

Regarding claim 2, Bacus discloses methods for immunoploidy analysis wherein the image of the cell is a digital representation of the cell (see abstract and column 17, lines 47-53).

Regarding claim 3, Bacus discloses methods for immunoploidy analysis wherein the cell is treated with an agent that selectively associates with DNA and emits a signal recorded as the DNA image parameter.

Regarding claim 4, Bacus discloses methods for immunoploidy analysis wherein the agent is a DNA stain (column 7, lines 55-59).

Regarding claim 5, Bacus discloses methods for immunoploidy analysis wherein the DNA image parameter is a light or radiation intensity (column 9, lines 51-57 and column10, lines 27-30).

Regarding claim 6, Bacus discloses methods for immunoploidy analysis wherein the DNA image parameter is electromagnetic radiation intensity provided at a particular wavelength or range of wavelengths (column 11, lines 5-10).

Regarding claim 7, Bacus discloses methods for immunoploidy analysis wherein estimating the total value of the DNA image parameter comprises summing a per pixel value of the DNA image parameter over all pixels in the region of the cell where DNA is deemed to be present (column 21, lines 62-67 and column 22, lines 1-15).

Regarding claim 8, Bacus discloses methods for immunoploidy analysis wherein the per pixel value of the DNA image parameter comprises a corrected per pixel intensity value (column 12, lines 34-43 and column 13, lines 10-26).

Claim 9, is similarly analyzed as claim 8 above.

Regarding claim 10, Bacus discloses methods for immunoploidy analysis wherein the corrected per pixel intensity value comprises the difference corrected for non-linearities in an image acquisition system used to produce the image of the cell (column 10, lines 47-59 and column 11, lines 10-26).

Claim 11, is similarly analyzed as claim 1 above.

Regarding claim 12, Bacus discloses methods for immunoploidy analysis further comprising classifying the cell into a cell cycle state based on the estimated value of total DNA (column 8, lines 45-52 and column 18, lines 44-54).

Regarding claim 13, Bacus discloses methods for immunoploidy analysis wherein classifying the cell into a cell cycle state comprises using a mixture model to operate on estimated values of total DNA for a population of cells (column 7, lines 59-64).

Regarding claim 14, Bacus discloses methods for immunoploidy analysis wherein the region of the cell where DNA is deemed to be present is the cell nucleus (column 5, lines 42-46).

Claim 15, is similarly analyzed as claim 1 above.

Claim 16, is similarly analyzed as claim 2 above.

Claim 17, is similarly analyzed as claim 3 above.

Claim 18, is similarly analyzed as claim 4 above.

Claim 19, is similarly analyzed as claim 5 above.

Claim 20, is similarly analyzed as claim 6 above.

Claim 21, is similarly analyzed as claim 7 above.

Claim 22, is similarly analyzed as claim 8 above.

Claim 23, is similarly analyzed as claim 9 above.

Claim 24, is similarly analyzed as claim 10 above.

Claim 25, is similarly analyzed as claim 11 above.

Claim 26, is similarly analyzed as claim 12 above.

Claim 27, is similarly analyzed as claim 13 above.

Claim 28, is similarly analyzed as claim 14 above.

Regarding claim 29, Bacus discloses methods for immunoploidy analysis comprising:

a memory or buffer adapted to store (column 11, lines 49-53), al least temporarily, an image of the cell (column 4, lines 58-62), in which image local values of a DNA image parameter correspond to amounts of DNA at the locations within the cell shown on the image (column 7, lines 40-46); and,

a processor configured or designed to estimate a total value of the DNA image parameter taken over at least a region of the cell where DNA is deemed to be present (column 9, lines 57-59 and column 4, lines 41-47).

Regarding claim 30, Bacus discloses methods for immunoploidy analysis further comprising an interface adapted to receive the image of the cell (column 10, lines 13-16 and column 11, lines 14-22).

Regarding claim 31, Bacus discloses methods for immunoploidy analysis further comprising an image acquisition system that produces the image of the cell (column 9, lines 51-53).

Claim 32, is similarly analyzed as claim 3 above.

Claim 33, is similarly analyzed as claim 5 above.

Claim 34, is similarly analyzed as claim 7 above.

Claim 35, is similarly analyzed as claim 8 above.

Claim 36, is similarly analyzed as claim 10 above.

Claim 37, is similarly analyzed as claim 29 above.

4. Claims 38-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhu et al (U S 5,710,022) in view of Bacus et al (U S 5,281,517).

Regarding claim 38, Zhu discloses nuclear mitotic phosphoprotein comprising:

from the image, extracting values of one or more mitosis indicator parameters that correspond to a cell division state of the cell (column 1, lines 61-66; column 4, lines 17-27 and column 19, lines 25-35); and,

classifying the cell as either mitotic, or interphase based upon the extracted values of the one or more mitosis indicator parameters (column 4, lines 48-58 and column 16, lines 60-63).

However, Zhu is silent about the specific details regarding the steps of:

receiving an image of a cell; and classifying the cell.

In the same field of endeavor, however, Bacus discloses methods for immunoploidy analysis comprising the steps of:

receiving an image of a cell (column 4, lines 58-62); and classifying the cell (column 10, lines 45-63).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use image of cell and cell classification as taught by Bacus in the system of Zhu because Bacus provides Zhu a system where a moderate number of inflammatory cells are present in a tumor. Thus using an antibody to leukocyte common antigen, the immunological marking can identify these inflammatory cells so they can be excluded from DNA assay, and also this system had an advantage which allowing the pathologist to use this subjective skills to separate the tumor cells from the non-tumor cells for DNA analysis.

Claim 39, is similarly analyzed as claim 2 above.

Claim 40, is similarly analyzed as claim 3 above.

Claim 41, is similarly analyzed as claim 6 above.

Claim 42, is similarly analyzed as claim 4 above.

Regarding claim 43, Zhu discloses nuclear mitotic phosphoprotein wherein the one or more mitosis indicator parameters include at least one of a variance in DNA concentration within the cell, the size of a region occupied by DNA within the cell, an average concentration of DNA within the cell, and a maximal concentration of DNA within the cell (column 8, lines 37-45).

Regarding claim 44, Zhu discloses nuclear mitotic phosphoprotein wherein the one or more mitosis indicator parameters include at least a variance in DNA concentration within the cell (column 19, lines 25-31).

Regarding claim 45, Zhu discloses nuclear mitotic phosphoprotein wherein classifying the cell as either mitotic or interphase comprises evaluating the one or more mitosis indicator parameters to determine a degree to which DNA within the cell has separated (column 17, lines 13-22).

Regarding claim 46, Zhu discloses nuclear mitotic phosphoprotein wherein classifying the cell as either mitotic or interphase comprises evaluating the one or more mitosis indicator parameters to determine a degree to which DNA within the cell has condensed into chromosomes (column 2, lines 41-51 and column 15, lines 44-54).

Regarding claim 47, Zhu discloses nuclear mitotic phosphoprotein wherein classifying the cell as either mitotic or interphase comprises evaluating the one or more mitosis indicator parameters to determine a degree to which DNA within the cell has concentrated into one or more discrete locations (column 16, lines 48-53).

Regarding claim 48, Zhu discloses nuclear mitotic phosphoprotein further comprising classifying a mitotic cell as pre or post anaphase (column 2, lines 41-51).

Claim 49, is similarly analyzed as claim 13 above.

Regarding claim 50, Zhu is silent about the specific details regarding the image of the cell shows locations where the DNA exists within the cell.

In the same field of endeavor, however, Bacus discloses methods for immunoploidy analysis comprising the step of image of the cell shows locations where the DNA exists within the cell (column 13, lines 1-3).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use locations where the DNA exists within the cell as taught by Bacus in the system of Zhu because Bacus provides Zhu a system where a moderate number of inflammatory cells are present in a tumor. Thus using an antibody to leukocyte common antigen, the immunological marking can identify these inflammatory cells so they can be excluded from DNA assay, and also this system had an advantage which allowing the pathologist to use this subjective skills to separate the tumor cells from the non-tumor cells for DNA analysis.

Claim 51, is similarly analyzed as claim 38 above.

Claim 52, is similarly analyzed as claim 39 above.

Claim 53, is similarly analyzed as claim 40 above.

Claim 54, is similarly analyzed as claim 41 above.

Claim 55, is similarly analyzed as claim 42 above.

Claim 56, is similarly analyzed as claim 43 above.

Claim 57, is similarly analyzed as claim 44 above.

Claim 58, is similarly analyzed as claim 45 above.

Claim 59, is similarly analyzed as claim 46 above.

Claim 60, is similarly analyzed as claim 47 above.

Claim 61, is similarly analyzed as claim 48 above.

Claim 62, is similarly analyzed as claim 49 above.

Claim 63, is similarly analyzed as claim 50 above.

Claim 64, is similarly analyzed as claim 29 above.

Claim 65, is similarly analyzed as claim 30 above.

Claim 66, is similarly analyzed as claim 31 above.

Claim 67, is similarly analyzed as claim 32 above.

Claim 68, is similarly analyzed as claim 43 above.

Claim 69, is similarly analyzed as claim 44 above.

Claim 70, is similarly analyzed as claim 46 above.

Claim 71, is similarly analyzed as claim 47 above.

Claim 72, is similarly analyzed as claim 50 above.

Claim 73, is similarly analyzed as claim 38 above.

Regarding claim 74, Zhu discloses nuclear mitotic phosphoprotein wherein the cell cycle phases into which the cell can be classified include G1, S, G2, and mitotic (column 1, loines 61-67 and column 2, lines 1-11).

Regarding claim 75, Zhu discloses nuclear mitotic phosphoprotein wherein the cell cycle phases into which the cell can be classified include G1, S, G2, pre-anaphase mitotic, and post-anaphase mitotic (column 2, lines 34-54).

Regarding claim 76, Zhu discloses nuclear mitotic phosphoprotein wherein classifying the cell comprises comparing at least one of the amount of DNA and the one or more mitosis indicator parameters to a model providing boundaries between certain cell cycle phases in parameter space (column 19, lines 26-36).

Claim 77, is similarly analyzed as claim 38 above.

Claim 78, is similarly analyzed as claim 13 above.

Claim 79, is similarly analyzed as claim 13 above.

Regarding claim 80, Zhu is silent about the specific details regarding the multiple sources are multiple wells on an assay plate.

In the same field of endeavor, however, Bacus discloses methods for immunoploidy analysis comprising the multiple sources are multiple wells on an assay plate (column 5, lines 25-28 and column13, lines 58-61).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use multiple sources are multiple wells on an assay plate as taught by Bacus in the system of Zhu because Bacus provides Zhu a system where a moderate number of inflammatory cells are present in a tumor. Thus using an antibody to leukocyte common antigen, the immunological marking can identify these inflammatory cells so they can be excluded from DNA assay, and also this system had an advantage which allowing the pathologist to use this subjective skills to separate the tumor cells from the non-tumor cells for DNA analysis.

Regarding claim 81, Zhu discloses nuclear mitotic phosphoprotein wherein the population used to generate the model is a collection of images of control cells having a known distribution of cell cycle phases (column 1, lines 48-53).

Claim 82, is similarly analyzed as claim 73 above.

Claim 83, is similarly analyzed as claim 74 above.

Claim 84, is similarly analyzed as claim 75 above.

Claim 85, is similarly analyzed as claim 76 above.

Claim 86, is similarly analyzed as claim 77 above.

Claim 87, is similarly analyzed as claim 78 above.

Claim 88, is similarly analyzed as claim 79 above.

Claim 89, is similarly analyzed as claim 80 above.

Claim 90, is similarly analyzed as claim 81 above.

Claim 91, is similarly analyzed as claim 29 above.

Claim 92, is similarly analyzed as claim 30 above.

Claim 93, is similarly analyzed as claim 31 above.

Claim 94, is similarly analyzed as claim 32 above.

Claim 95, is similarly analyzed as claim 43 above.

Claim 96, is similarly analyzed as claim 46 above.

Claim 97, is similarly analyzed as claim 7 above.

Claim 98, is similarly analyzed as claim 94 above.

Claim 99, is similarly analyzed as claim 8 above.

Claim 100, is similarly analyzed as claim 9 above.

Claim 101, is similarly analyzed as claim 38 above.

Regarding claim 102, Zhu discloses nuclear mitotic phosphoprotein wherein the population of cells includes cells treated under control conditions (column 7, 42-47 and column 16, lines 36-43).

Regarding claim 103, Zhu discloses nuclear mitotic phosphoprotein wherein the population of cells includes a first set of cells treated with a first concentration of a

biologically active agent and a second set of cells treated with a second concentration of the biologically active agent (column 2, lines 1-12 and column 5, lines 39-48).

Regarding claim 104, Zhu discloses nuclear mitotic phosphoprotein wherein the population of cells further includes a third set of cells treated under control conditions (column 2, lines 12).

Claim 105, is similarly analyzed as claim 13 above.

Claim 106, is similarly analyzed as claim 13 above.

Claim 107, is similarly analyzed as claim 74 above.

Claim 108, is similarly analyzed as claim 75 above.

Claims 109, 110 and 111 are similarly analyzed as claim 101 above.

Claim 112, is similarly analyzed as claim 102 above.

Claim 113, is similarly analyzed as claim 103 above.

Claim 114, is similarly analyzed as claim 104 above.

Claim 115, is similarly analyzed as claim 105 above.

Claim 116, is similarly analyzed as claim 106 above.

Claim 117, is similarly analyzed as claim 107 above.

Claim 118, is similarly analyzed as claim 108 above.

Claim 119, is similarly analyzed as claim 109 above.

Claim 120, is similarly analyzed as claim 110 above.

Other prior art Cited

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Sabry (U S 6,615,141 B1) discloses data base system for predictive cellular bioinformatics.

Silver (U S 6,078,681) discloses analytical imaging system and process.

Bacus et al (U S 5,016,283) disclose methods and apparatus for immunoploidy analysis.

Singer et al (U S 5,985,549) disclose non-isotopic in-situ hybridization method for detection of nucleic acids.

Contact Information

6. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to ABOLFAZL TABATABAI whose telephone number is (703) 306-5917.
The Examiner can normally be reached on Monday through Friday from 9:30 a.m. to 7:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Mehta Bhavesh M, can be reached at (703) 308-5246. The fax phone number for organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Abolfazl Tabatabai

Patent Examiner

Group Art Unit 2625

March 1, 2004

Jayanti K. Patel
Primary Examiner